

REMARKS

Claims 20 – 32 are pending. Claims 20 – 21 were previously withdrawn. No amendment has been made.

Claim rejections - 35 U.S.C. §112

Applicants thank the Examiner for withdrawing the rejections of the claims under 35 U.S.C. 112, first paragraph.

Claim rejections - 35 U.S.C. §103

Applicants respectfully traverse the obviousness rejections of claims 22-32 over Weigel et al (US 6,991,921) in view of Sohn et al (US 6,444,805), further in view of Fischer et al (2000 Transgenic Research 9: 279-299), and further in light of Xia (US 6,395,965).

None of the cited references, alone or in combination, teaches or suggests a method of producing hyaluronic acid comprising a step of transforming a plant cell using an expression recombinant vector comprising (i) a DNA encoding hyaluronic acid synthase or (ii) a DNA encoding a polypeptide having an amino acid sequence of the hyaluronic acid synthase **wherein the hyaluronic acid synthase is derived from a chlorella virus**, as recited in claim 22.

Applicants have found, surprisingly, that only chlorella virus-derived hyaluronic acid synthase (HAS) genes, but not those from bacteria or mouse, can impart a plant or a plant cell with the ability to produce hyaluronic acid. These unexpected results were presented in the Declaration filed November 6, 2007. The Office Action, however, does not indicate that the Declaration has been considered. Applicants hereby submit a revised Declaration with the additional data showing *in vitro* HAS activity in the crude membrane fraction obtained from plant cells transformed with an HAS gene from chlorella virus, bacterial, or mouse (Table 1). The revised Declaration demonstrated that only a plant or a plant cell transformed with a HAS gene derived from a chlorella virus, but not those transformed with a bacteria or mouse HAS gene, exhibited HAS activity or produced hyaluronic acid (page 2, second paragraph; Table 1; Figs A and B). Because a plant or plant cell transformed with an HAS gene from bacterial or mouse did not acquire any HAS activity, an ordinary skilled in the art would have expected that a chlorella virus-derived hyaluronic acid synthase would not work in a plant or plant cell. Therefore, one of ordinary skill in the art would not have had a reasonable expectation of success in establishing a

method of producing hyaluronic acid by transforming a plant cell with a chlorella virus-derived HAS gene, as recited in claim 22. The attached Declaration shows that the method of claims 22-32 can achieve unexpected results.

Indeed, none of the cited references teaches or suggests which HAS gene can be used to transform a plant cell to produce hyaluronic acid in a plant. The Examiner acknowledged that “Weigel et al do no teach the transformation of plants using recombinant expression vector or the said construct further comprising a tissue or organ specific promoter.” Office Action, page 3, lines 17-19. But the Office Action contends that “Weigel et al teach the production of hyaluronic acid comprising a chlorella virus-derived hyaluronic acid synthase and transforming a streptococcal bacterium and isolating the hyaluronic acid from the bacterium (see claims and Figure 12 for example).” Page 3, lines 13. Figure 12 of Weigel, however, is a demonstration of the synthesis of authentic hyaluronic acid by the recombinant seHAS, which is *Streptococcus equisimilis* hyaluronate synthase, not a chlorella virus-derived HAS. See column 1, lines 37-38; column 11, lines 58-59. Weigel does not teach or suggest a step of transforming a plant cell using an expression recombinant vector comprising a chlorella virus-derived hyaluronic acid synthase gene, as recited in claim 22. The deficiency of Weigel is not cured by Sohn, Fischer, and Xia. None of these references discloses, explicitly or implicitly, transformation of a plant or a plant cell with an expression recombinant vector comprising a hyaluronic acid synthase derived from a chlorella virus, as required by claim 22.

For at least the reasons stated above, claims 22-32 would not have been obvious over Weigel in view of Sohn, further in view of Fischer, and further in light of Xia. Withdrawal of the rejections is respectfully requested.

CONCLUSION

The Examiner is encouraged to contact the undersigned regarding any questions concerning this amendment. In the event that the filing of this paper is deemed not timely, applicants petition for an appropriate extension of time. The Commissioner is authorized to debit Deposit Account No. 11-0600 the petition fee and any other fees that may be required in relation to this paper.

Respectfully submitted,

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